REMARKS

Applicant has reviewed and considered the Office Action mailed on December 3, 2002, and the documents cited therein.

Claims 1-35 and 49-61 are cancelled, claims 36, 39, 43, 45, 47 and 62 are amended, and claims 63-78 are added. As a result, claims 36-48 and 62-78 are now pending and under examination in this application.

Solely for reasons for expediting prosecution, previously dependent claims 36, 39, 43 and 45 have been rewritten as independent claims.

Claims 47 and 62 have been amended to change dependencies.

New claims 63-65 and 76-78 are supported, for example, by the specification at page 13, lines 1-25, page 16, lines 5-22, and by Figures 2, 3, and 4.

New claims 66-71 are supported, for example, by originally-filed claims 34 and 47-48.

New claims 72-75 are supported, for example, by the specification at page 6, lines 5-11.

No new matter has been added.

The Rejection of the Claims under 35 U.S.C. § 103(a)

The Examiner rejected claims 34-35, 37-38 and 47-48 under 35 U.S.C. § 103(a) as being unpatentable over Schwarze *et al.* (*Science* 285:1569-1572 (1999)) in view of Ghodsi *et al.* (*Exp. Neuro.* 160:109-116, (1999) or *Hum. Gene Therapy* 9:2331-2340 (1998)). Thus, the Examiner has implied that claims 36, 39-46 and 62 are free of the cited art. As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

Solely for reasons for expediting prosecution, Applicant has cancelled claims 34 and 35.

Applicant has rewritten claim 36 as an independent claim. Claims 37-38, 47-48 and 62 depend directly or indirectly from claim 36, as does new claim 72. The Examiner has implied that claim 36 is free of the cited art. Therefore, claims 37-38, 47-48, 62 and 72 are also free of the cited art.

Previously dependent claims 39, 43 and 45 have been rewritten as independent claims. New claims 63-71 and 73-78 depend directly or indirectly from claims 39, 43 or 45. The

Examiner has implied that claims 39, 43 and 45 are free of the cited art. Therefore, claims 63-71 and 73-78 are also free of the cited art.

Thus, because the pending claims are free of the cited art, the rejection of the pending claims under 35 U.S.C. § 103(a) should be withdrawn.

The Rejection of the Claims under 35 U.S.C. § 112, First Paragraph

The Examiner rejected claims 34-48 and 62 under 35 U.S.C. § 112, first paragraph, alleging that the specification, while being enabling for a β-galactosidase fused to a PTD sequence, does not reasonably provide enablement for all types of proteins fused to PTD. As a point of clarification, the Examiner on page 3 of the Office Action mailed 12/03/02 used the term "β-galactosidase," whereas the working example in the present specification is was to β-glucuronidase (*i.e.*, a lysosomal enzyme). As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

First, the Examiner states on page 3 of the Office Action that one of skill in the art would undergo undue experimentation to practice the invention commensurate in scope to the claims because "the construction of fusion proteins is not a simple task." Applicant respectfully disagrees with the examiner regarding the ease of making fusion proteins. At this point, many kits are commercially available for artisans to easily generate fusion proteins. For example, the Invitrogen, Clonetech and Stratagene companies provide kits for generating fusion proteins. Thus, it is quite routine for artisans to generate fusion proteins. Once the fusion protein is made, the investigator would easily be able to perform a screening assay to test the biological activity of the fusion protein. An investigator wishing to modify a protein with a PTD would know how to assay for its biological activity, or else he or she would not be studying it. Therefore, even if some experimentation was needed in order to test the possible new proteins that would be covered by Applicant's application, it would not require undue experimentation to generate and screen even very large numbers of fusion proteins in view of teaching of the present specification.

Second, the Examiner states on pages 3-4 of the Office Action that even if one was successful in generating an enzyme that was functional *in vitro*, one would not know if it was functional *in vivo*. The Examiner states that the "expression of a fusion protein in vitro does not confer in vivo success, and as such one of skill in the art would be forced to experiment to determine if the fusion of an enzyme to a PTD would work effectively." The Examiner has provided no support for this statement. Applicant asserts that there is no *a priori* reason why a protein that has biological activity *in vitro* would no longer have that activity *in vivo*.

Applicant requests that these rejections under 35 U.S.C. § 112, first paragraph, be withdrawn.

Conclusion

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (612-373-6961) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,
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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Box AF, Commissioner of Patents, Washington, D.C. 20231, on this 3 day of April, 2003.

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Name

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